Disparities in Infant Mortality: What's Genetics Got to Do With It?

Since 1950, dramatic advances in human genetics have occurred, racial disparities in infant mortality have widened, and the United States' international ranking in infant mortality has deteriorated. The quest for a "preterm birth gene" to explain racial differences is now under way.

Scores of papers linking polymorphisms to preterm birth have appeared in the past few years. Is this strategy likely to reduce racial disparities? We reviewed broad epidemiological patterns that call this approach into question.

Overall patterns of racial disparities in mortality and secular changes in rates of prematurity as well as birthweight patterns in infants of African immigrant populations contradict the genetic theory of race and point toward social mechanisms. We postulate that a causal link to class disparities in health exists. (*Am J Public Health*. 2007;97:1191–1197. doi:10.2105/AJPH.2005.068387)

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THE AVAILABILITY OF information on molecular genetics has exploded in recent decades. From the description of the double helix by Watson and Crick in 1953 to the sequencing of the human genome in 2003 and the beginnings of genomic medicine, scientific knowledge has accumulated at a breathtaking pace. Over the same decades, the United States, the world leader in newborn intensive care, fell from 6th to 27th in its international standing for infant mortality rate. At the same time, the racial gap for infant mortality in the United States has widened. The rate of death in the first year of life for Black infants increased from 1.6 times to 2.3 times the rate of White infants.[1,2] The worsened national statistics for infant mortality are not just the result of including the poor outcomes for Blacks. In 2001 the infant mortality rate for White infants born in the United States was 5.7 per 1000 live births, which would give that subgroup a rank of 23rd in the world, not much better than 27th. The US rate for Whites was more than twice as high as the country with the best record in the world: Singapore, at 2.4 deaths per 1000 live births.[2]

Observation of these trends should give pause to those who are tempted to approach public health problems with strictly technological solutions, of which genomic medicine is the latest example. Despite having the world's most advanced technology, the United States continues to fall farther behind other nations in health outcomes. The widening racial disparity in infant mortality during the era of molecular genetics should also prompt skepticism that genetic research holds the key to understanding and eliminating the disparities, a goal of the Healthy People 2010 objectives.[3] Indeed, it has been argued by anthropologists for years that "race" has little or no meaning as a genetic category but rather derives all its usefulness from its very clear social, political, cultural, and historical meaning.[4,5] These social meanings of race have clear public health implications.[1,6–8] We evaluated the expected utility of 2 approaches to racial disparities: one based on race as a proxy for geographic ancestry and genetics, and the other based on race as a social construct.

"RACE," GEOGRAPHIC ANCESTRY, AND HEALTH

"Race" in its traditional genetic conceptualization has been undermined by a wealth of information from molecular biology over the past 30 years. Most human genetic variation (90% to 95%) is found within the population of any continent, with only an additional 5% to 10% accounted for by differences in gene frequencies between continental populations.[5,9] Patterns of human variation reflect our evolutionary history as a young species (anatomically modern *Homo sapiens*), originating in Africa roughly 200 000 years ago. For more than half of the intervening time, all modern humans lived in Africa, with smaller founding populations arriving in Asia and Europe within the past 80 000 to 50 000 years.[5,10]

When hundreds of variable sites in the genome are sampled, geographical structures of diversity (statistical associations of DNA markers with populations native to different geographic locations) can be discerned, roughly corresponding to continental barriers to ancient migrations, such as oceans or mountain ranges. These statistical clusters do not fit into the traditional, essentialist concept of "races." Attempts to conflate such constructs with traditional racial classification impede a more sophisticated understanding of genomic diversity.[11,12] Geographical structuring is inferred from multiple neutrally varying sites. By contrast, medically relevant loci are often subject to strong natural selection or to genetic drift of rare alleles following population bottlenecks (evolutionary events in which a significant percentage of a population or species is killed or otherwise prevented from reproducing) and the populations of interest do not necessarily coincide with continental populations.[12,13]

Differences in allele frequencies between geographic populations have well-known effects on the incidence of uncommon diseases such as cystic fibrosis and sickle cell anemia.[14] Whether they will turn out to have parallels in common complex diseases remains to be demonstrated.[15–17] There is as yet no complex disease for which

the genetic components are completely or even largely understood, but the popular genetic conception of "race" in medical research in the United States takes genetic differences between Whites and Blacks as a starting point.

Recently, researchers have suggested adding preterm birth to the list of such complex conditions as heart disease, hypertension, and diabetes.[18,19] The hunt is on for "preterm birth genes" that can explain the disparity in prematurity and infant mortality between Blacks and Whites. The March of Dimes Research Agenda on Prematurity lists genetic factors as the second rubric under the category "racial/ethnic disparities."[20] A typical rationale for the genetic approach is that "African American women suffer twice the rate of preterm birth compared with Caucasians even when confounding social and economic variables are controlled for."[19(p57)] Can all or even most of the multifaceted social, economic, political, and historical effects of racial discrimination be adequately "controlled for" with the variables commonly measured?[1,21] Clearly some investigators believe they can.

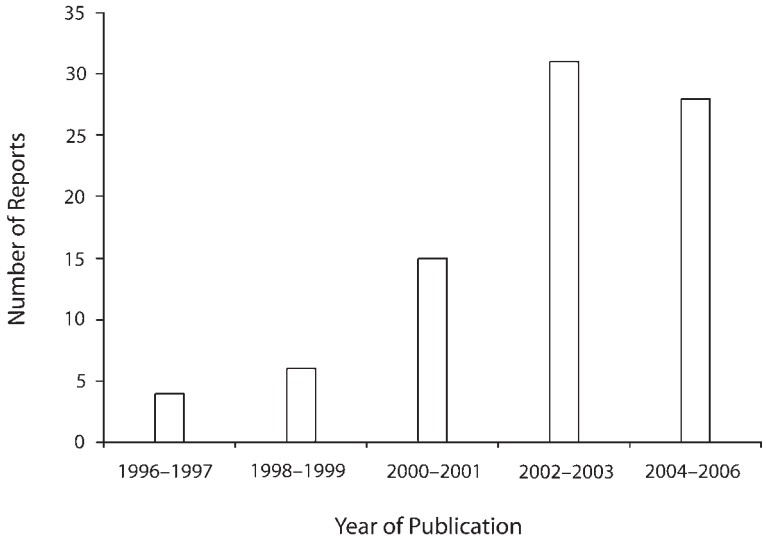
Reports of polymorphisms associated with adverse birth outcomes appear to be growing exponentially at this time (Figure 1). Fiscella reviewed this literature extensively and published his findings in late 2005.[22] He tabulated 70 reports describing 32 different genetic variants putatively implicated in the risk of preterm birth along with racial differences in gene frequency. A PubMed search in February 2006 identified 14 additional reports.[23–36] Of the combined total of 84 articles, 59 have been published since 2002. Does existing population health evidence support this increasingly intense pursuit of a genetic basis for racial disparities in birth outcomes?

FROM THE NEW DEAL TO BIDIL

It can be argued that social and economic forces, rather than scientific evidence, underlie this proliferation of genetic research on racial disparities. Current social and political discourse in this country favors individual-level and technology-based solutions over extensions (or even maintenance) of the social contract implicit in US politics since the New Deal. More and more, a business model dominates medical research, with more than 20% of the genes in the human genome now under patent.[37] In 2005, the first "ethnic drug," BiDil, was approved by the US Food and Drug Administration for treatment of heart failure specifically in Blacks.[38,39] The licensing of this product is seen by many as the first of many pharmaceuticals that will be tailored to different physiology in different people—genomic medicine. And of course, people belonging to different "races" will be assumed to differ at the genome level, providing distinct niche markets. Sociologist Troy Duster predicts that, because "race is such a dominant category," such endeavors in biomedicine "can leave [their] own indelible mark once given the temporary imprimatur of scientific legitimacy by molecular genetics."[40(p1050)] Given the risk of wasting large amounts of scientific effort and reinforcing popular misperceptions of "race," do the existing population data justify this quest?

RACE AND MORTALITY

An overview of racial disparities in birth outcomes will help to put the current research agenda into perspective. The 5 leading causes of death in the first year of life in the United States for Black and White infants[41] are shown in Table 1. Table 1 also shows the Black-to-White rate ratios of infant death for each of the major causes. These ratios range from a high of 3.9 for "disorders related to short gestation" to a low of 1.2 for "congenital malformations." It is noteworthy that the mortality disadvantage of Black Americans is observed across all of the major categories of infant death. A similar pattern is seen in adults. Of the 10 leading causes of death, Blacks have lower death rates for only 2: chronic lung disease and Alzheimer disease.[42] It is highly unlikely for any given population to have concentrated multiple deleterious mutations in such a way that they are at higher risk for almost all of the common complex disorders on a genetic basis. Social, economic, and cultural processes, on the other hand,



Source. All articles before 2003 and 45 of the 59 from 2003 onward were cited in Table 1 in Fiscella.[22] The remaining 14 articles[23-36] were obtained from a PubMed search in February 2006.

FIGURE 1—Quantity of reports describing polymorphisms putatively implicated in the risk of preterm birth or other adverse birth outcomes.

TABLE 1—Cause-Specific Infant Death Rates: United States, 2000

Causes of Infant Death	Death Rate[a]			
	Total	White	Black	RR
All causes	688.9	571.2	1347.7	2.4
Congenital malformations (Q00–Q99)	141.8	138.5	167	1.2
Disorders related to short gestation (P07)	108.4	74.7	293.6	3.9
Sudden infant death syndrome (R95)	62.1	51.8	122.1	2.4
Maternal pregnancy complications (P01)	34.3	26.1	80.5	3.1
Complications of placenta, cord, membranes (P02)	25.7	22.3	45.6	2.0

Note. RR = rate ratio (Black to White). Data are from *National Vital Statistics Reports.*[41] Codes (in parentheses) are from *International Classification of Diseases, 10th Revision.*
[a]Per 100 000 live births.

could reasonably be hypothesized to cause adverse impacts on historically disadvantaged groups in a multifaceted and multilayered manner.[1,6,8,21] Indeed, social-class gradients have been demonstrated for a variety of diseases in all age groups since the classic studies of the 19th century.[43(p123–137),44(p109)] A contemporary report from the United Kingdom reveals that the same pattern persists today: a significant social-class mortality gradient, as well as significant gradients for 15 of the 17 specific causes of child morbidity.[45]

BIRTHWEIGHT AND ANCESTRY

Birthweight, a commonly used proxy for gestational maturity, is the most important determinant of infant mortality differences between Whites and Black Americans. Most of the Black–White gap in first-year mortality is attributable to the higher rate of Black infants born at very low birthweight (less than 1500 g; 3 times that of White infants), essentially all of whom are preterm.[46] Short gestation is tightly linked with low birthweight but is more difficult to measure, because it involves an estimate based on the recall of menstrual history as opposed to a straightforward measurement made by hospital staff. The superior reliability of birthweight as a proxy for gestational maturity is especially apparent at the population level.[47,48] Researchers point out the persistence of a racial birthweight disparity after having controlled for various social or environmental risk factors.[19,49] Do population patterns of birthweight support a genetic basis?

One feature of population patterns of preterm or low-birthweight births that is at odds with genetic explanations of population differences is secular change. Average birth weights have risen in populations native to Japan, Pakistan, and Southeast Asia, among others, following either economic changes within the country of origin or immigration to more affluent societies.[50–52] Similarly, birthweights in the state of Illinois—within both White and Black families—increased from 33 g to 74 g over the generation from the 1960s to the 1990s.[53] More recently the National Center for Health Statistics reported that the rates of singleton preterm births changed significantly between 1989 and 1996 for both Whites and Blacks.[54] Population changes in phenotype caused by genetic drift or natural selection occur over tens of thousands of years, not over decades. Clearly these changes over brief periods of time must have an environmental, not a genetic, basis.

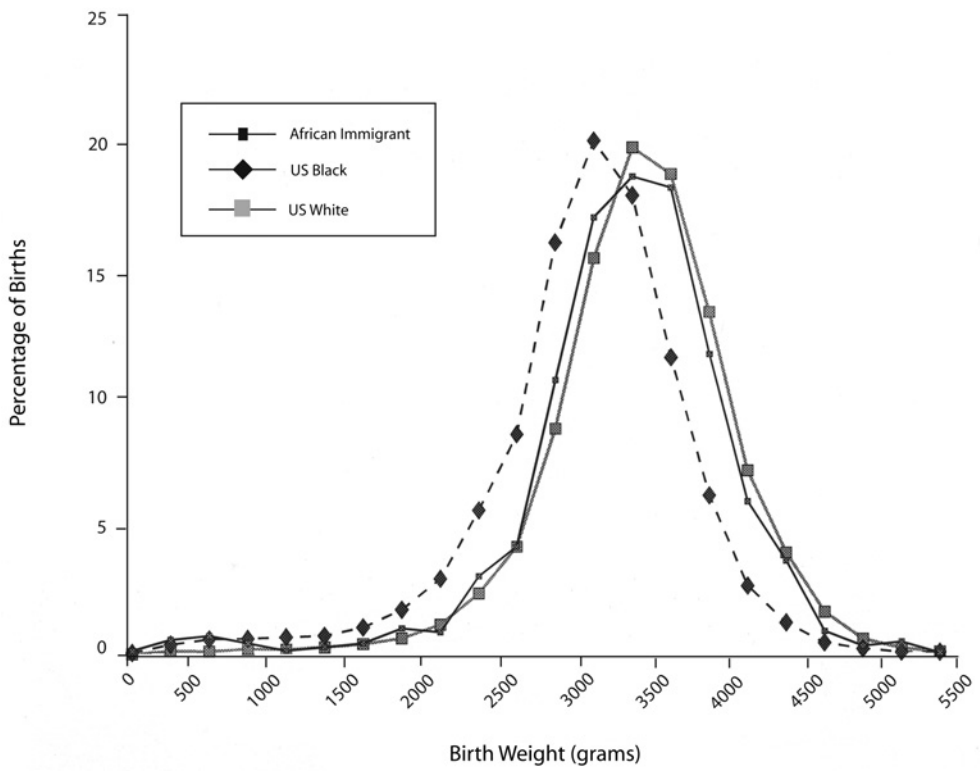
Perhaps the most direct test of the hypothesized linkage between continent of ancestry ("race") and birthweight was a comparison of birthweights among 3 groups of women delivering in Illinois over a 15-year period—US-born White women, US-born Black women, and African-born Black women.[55] Earlier research showed that US Blacks have significant European genetic admixture. If birthweight differences between US Blacks and Whites in North America were determined by different frequencies of alleles responsible for low birthweight and these "low birthweight genes" were derived from African populations, then the birth weight difference should be most pronounced in African women, less so in US Blacks, and least in women with largely European ancestry (so-called "Whites."). What we found was quite different. The overall birthweight distributions for infants of US-born White women and African-born women were almost identical, with US-born Black women's infants comprising a distinctly different population, weighing hundreds of grams less (Figure 2). Black women born in the United States also experienced higher rates of very low birthweight than either the White or African-born women once appropriate confounders were controlled.[55]

We performed a similar analysis of births to Black Caribbean women immigrants to the United States and again found that those women gave birth to infants hundreds of grams heavier than the infants of US-born Black women.[56] A recent report from Portugal[57] showed similar findings, except that the birthweights of the infants of African-born women in Portugal were actually somewhat higher than the weights of both groups of Portuguese-born women—those of African and of European ancestry.

HEALTHY IMMIGRANTS OR UNHEALTHY SOCIETY?

The possibility exists that the phenomenon observed in these groups of women migrating from majority-Black countries in Africa and the Caribbean represents a "healthy immigrant" effect, similar to that described for other populations.[58] We explored this hypothesis in a study of the birthweight patterns in the generation after women migrated from African or Caribbean countries to the United States. Our findings again contradicted predictions based on genetic race. We analyzed the intergenerational birthweight patterns among the descendants of US-born and foreign-born White and Black women.[59] Recent European immigrants to the United States gave birth to girls of similar birthweight to the girls born into established European American (White) families, and these girls grew up to have daughters whose average birthweight was higher than their own. This is the same pattern of rising birthweights over a generation that we had described previously in Illinois.[52]

Black African and Caribbean immigrants, on the other hand, gave birth to girls who were heavier than the girls born into established Black American families. Most striking, these first-generation Black girls grew up in the United States and went on to have daughters whose birthweights were lower on average than their own weights had been at birth. This generational trend



Source. Reprinted with permission from David and Collins.[55]

FIGURE 2—Birthweight distributions of 3 Illinois subpopulations.

is opposite to that seen in the nonimmigrant population and opposite the trend in European immigrant families.[59]

It is possible that a "healthy immigrant" effect could exist for Africans and not for Europeans, given the more stringent visa requirements for African immigrants.[60] However, if such immigration selection were in some way related to genetics, the pattern should persist into the next generation. That is not what we observed. Our findings were not readily explained by any genetic mechanism but rather suggested that negative effects of minority status are cumulative through the life course from fetus to childbearing woman.

An overview of the pattern of racial disparities in birth outcomes in the United States can be summarized as follows. Like health disparities in US adults, the disadvantage in cause-specific death rates for Black infants compared with White infants is distributed across nearly all causes. Racial disparity in infant deaths is highest for deaths related to prematurity and lowest for birth defects and chromosomal disorders. The pattern of low birthweight and prematurity in the population is not static but shows significant secular change over a generation or less. The low birthweights typical for Black infants in the United States or Portugal are not seen among infants born to recent immigrants from Africa or the Caribbean. After a generation of minority status, however, the birthweights in these families approximate those in the established Black minority population of the respective country.

DISPARITIES RESEARCH GROUNDED IN A SOCIAL CONCEPTION OF RACE

As suggested at the outset, the epidemiological evidence suggests that public health planners look to social and environmental rather than genetic differences between Black and White women in the campaign to eliminate health disparities. As Rudolph Virchow put it when considering mass diseases affecting German society in the 1860s, these conditions "indicate disturbances rooted in our social and governmental institutions, [and] hence [are] preventable."[61(p5)] Even as biotechnology firms were applying for gene patents and molecular biologists were formulating their first studies in pursuit of a "preterm-birth gene" in Black women, another approach was being formulated. This approach to racial disparities research turned from "race" to "racism." Stimulated by a series of conferences convened by the Centers for Disease Control and Prevention under the leadership of Diane Rowley and Carol Hogue in the early 1990s,[62,63] a new picture of Black–White differences began to emerge: race as a social category is associated with a complex array of disparities in life experience in our highly racialized society.

Geronimus, who was first to point out the deterioration of birth outcomes of Black women as they age from adolescence into their 20s, the so-called "weathering" phenomenon, noted the elevated and rising levels of lead in the blood of Black women living in polluted neighborhoods.[64,66] Similarly, we described adverse birth outcomes for Black women exposed to neighborhood violence,[66] other unsatisfactory aspects of their residential environments, and stressful life events.[67] The subjective reports of increased levels of life stress described by Black women compared with White women fit with published statistics. To take 2 striking examples, Blacks—both women of childbearing age and their partners—are more than twice as likely to be in the US Army[68,69] and 7 times as likely to be incarcerated[69,70] as Whites. In our case–control study of Black women giving birth in 2 Chicago hospitals, a remarkably high 16% reported incarceration of their partner during the pregnancy.[71] In addition to these examples of community- and institutional-level effects of racism, recent studies by

our group[72] and others[73–75] demonstrated similar deleterious effects on the interpersonal level. These studies showed an adverse impact of perceived racial discrimination on the birth outcome for Black women.

ELIMINATING RACIAL DISPARITIES TO REDUCE WHITE INFANT MORTALITY

The importance of a sociopolitical approach to understanding and eliminating racial health disparities extends beyond its potential benefits for Blacks in America. As noted, Whites in America also fare poorly compared with people in other countries, despite the United States having the world's largest per-capita expenditure on medical care.[76] The US racial gap in infant mortality and the gap between the United States and the world's leader in infant mortality reduction, Japan, have increased in tandem over the past half century.[1] Is there a causal pathway that could explain this tight temporal correlation? The missing concept to formulate this pathway is social class. Health statistics in the United States record categories of ethnicity but not social class.[15] However, an extensive literature documents the impact of social class on health in other wealthy, industrialized societies, including on infant mortality.[77–80] In a recent cross-sectional study of 16 wealthy member countries of the Organisation for Economic Co-operation and Development, Muntaner et al. analyzed the impact of national-level politics on birth outcomes. The authors reported that "the rates of low birthweight and infant deaths from all causes were lower in those countries with more voter turnout, more left votes, more left members of parliament, more women in government, a stronger social pact and various aspects of the welfare state, and low income inequality, as measured in a variety of ways."[81(p651)]

Understanding health outcomes for the majority population in the United States requires a model that incorporates race both as a social construct and as a social class. We propose a model that links the 2 by the mechanism of class power. That is, the political influence exercised by an economic class depends on its political unity in pursuing its class agenda. To the extent that racial identity inhibits class identity, it also reduces class unity and class political power. This process has been labeled "divide and conquer." We speculate that the unique history of race in the United States has led to a situation in which political unity and influence of the working classes—ordinary wage earners—is relatively low, as indicated by the international comparison reported by Muntaner et al.[81]

IMPLICATIONS FOR HEALTH DISPARITIES

Our national history includes the decimation of one ethnic group and the enslavement of another. A different economic and social history was more common for European colonies. In India, for example, the English mercantile class exploited colonial laborers thousands of miles from the home country, unseen by the average English workingman. By contrast, Africans brought to North America labored alongside "White" servants, pressed into service from the streets of London or Bristol. This necessitated a set of ideological justifications and supporting institutions. The laws preventing intermarriage between "races," forbidding voting or land ownership by Africans, and otherwise discriminating against them came into being in the late 1600s, a generation or more after the first Africans landed in the colonies. Bennett[82] argues that these measures prevented unified rebellions by Black and White plantation laborers. The very terms "Black" and "White" came into use—replacing African and Englishman, (or Christian)—only in the late 1600s. By these mechanisms African Americans were placed in a special social category where they contributed disproportionately to the country's wealth and acquired disproportionately little of it, a situation that began in the 17th century and continues today.[82,83]

No other modern nation shares our unique history. This past has led to the "peculiar institutions" of present-day US politics. As virtually the only industrialized country that has no labor party and no universal health care, our politics are indeed unusual. The speculation that our nation's history of race relations has led to our lack of class-based political institutions derives from the fact that popular culture and consciousness revolve around racial identity in the United States. Although racial ideologies have had[84,85]—and continue to have[86]—their own ugly history in Europe and elsewhere, there is no other industrialized nation where racial politics have been so dominant and consistent over time as in the United States.[87(p21ff)]

To be understood, the renewed interest in "race" as a genetic concept must be viewed in this context: scientific discovery and technologic advancement proceed according to their own dynamic of discovery, but scientists are part of society and subject to its political and cultural influences. The yearning for simple solutions to irreconcilable contradictions within a class-stratified society such as the United States has led to the recurrent reinvention of the concept of genetic "race"[88–90] despite abundant scientific evidence against it. It would almost appear that the idea is essential to the maintenance of class society as we know it.

In which direction does this point us in the ongoing effort to eliminate the glaring and shameful health disparities—racial and otherwise—that afflict our population? We can take encouragement from 2 observations. First, poor health outcomes for Blacks are inextricably connected to poor health in the US majority population relative to other affluent countries. This may seem like more bad news, but viewed from a different perspective it means that the objective basis exists for broad political unity to change the status quo. Second, despite the cultural influences that promote racial identity,[91] popular attitudes have shown movement toward breaking down racial separation,[92] with the number of mixed marriages increasing tenfold since 1960, now accounting for 4% of couples.[93] Thus, social class unity—across racial lines—could develop over time, making possible deep political change.

Researchers, especially those in public health and epidemiology, can help guide reform efforts. In the attempt to reduce adverse infant outcomes, detailed comparisons of the United States and other countries will be required,[94] as well as studies

that link health outcomes to explicit social, economic, and political processes.[95–97] Our evidence suggests that a redirection of disparities research will come as part of a more profound change, a change necessary to improve the health of the entire population. ■

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